

## REMARKS

Claims 1, 4-34, 36, 45, 46, 86-90, 157-181, 183, 212, 213, 263-267 and 280-296 were pending in the application. In the Office Action mailed September 11, 2007, claims 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265, 280-283, and 293-296 are rejected (claims 46, 88, 212-213 and 266-267 having been withdrawn from consideration as drawn to non-elected species). Claims 1, 7-9, 14-29, 31-34, 36, 45, 46, 86, 89, 90, 212, 263, 264, 280, 284, 285, and 293-296 have been amended to clarify the claimed invention.

Claim 1 has been amended to recite “expression levels of exon variants of a plurality of different genes in the genome of an organism in a cell sample derived from said organism” and “a plurality of different variants of an exon of a gene, for each gene in said plurality of different genes.” Support for the amendments is found, for example, at page 6, line 21 through page 7, line 13 of the specification.

Claim 1 also has been amended to recite steps involving use of a positionally addressable array, and to recite that the plurality of polynucleotide probes on the array comprises “a probe that specifically hybridizes to one of said different variants of an exon of a gene, for each gene in said plurality of different genes.” Support for the amendments is found, for example, at Figure 1; page 7, line 28 through page 8, line 12; page 9, lines 21-28; page 20, lines 19-33; page 38, lines 9-26; and page 48, lines 15-27 of the specification. Claim 1 also has been amended to recite levels of hybridization between probes and RNAs or nucleic acids in the cell sample indicate the nucleic acid expression levels of said plurality of different variants. Support for the amendment is found, for example, at page 48, lines 15-27 of the specification.

Support for the amendments to claims 28 and 29 is found, for example, at page 38, lines 1-4 of the specification.

Support for the amendment to claim 31 is found, for example, at page 26, lines 17-19 of the specification. Claim 33 has been amended to correct a grammatical error.

Support for the amendments to claims 89 and 90 is found, for example, at page 6, line 21 through page 7, line 13 of the specification.

Claim 264 has been amended for clarity of language and to be consistent with the language of claim 1.

Claim 280 has been amended to add a dependency upon claims 263 and 264. Support for the amendment is found, for example, at page 8, lines 5-35 (particularly lines 20-23) of the specification.

Claims 284 and 285 have been amended to be consistent with the language of claim 1. Support for the amendments to claims 284 and 285 is found, for example, at page 6, lines 1-2; page 6, line 21 through page 7, line 13; page 7, line 28 through page 8, line 12; page 20, lines 19-33; page 38, lines 9-26; and page 48, lines 15-27 of the specification.

Claims 293-296 have been amended for clarity of language and to be consistent with the language of claim 1.

Claims 4-6, 10-13, and 30 are canceled without prejudice.

Claims 7-9, 13-27, 45, 46, 86, 212, 263, 264, and 293 have been amended to remove dependency upon the canceled claims.

No new matter has been added by the amendments.

Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

#### **APPLICANTS' INTERVIEW SUMMARY**

Applicants thank Examiner Frank Lu for the courtesies extended during the telephone interview on October 18, 2007 (hereinafter "the First Interview") with Applicants' representatives Adriane M. Antler and Stephanie X. Wang. During the First Interview, Ms. Antler requested clarification of the bases for the rejection under 35 U.S.C. § 112, first paragraph, in the Office Action mailed September 11, 2007 (hereinafter "the Office Action"). The Examiner indicated that he would be willing to discuss the rejection in a couple of weeks.

Applicants also thank Supervisory Patent Examiner ("SPE") Ram Shukla and Examiner Lu for the courtesies extended during the telephone interview on October 18, 2007 (hereinafter "the Second Interview") with Applicants' representative Adriane M. Antler. During the Second Interview, SPE Shukla suggested that Applicants amend claim 1 in a manner that has been included in the amendments made hereinabove.

Applicants further thank SPE Shukla and Examiner Lu for the courtesies extended during the telephone interview on October 23, 2007 (hereinafter "the Third Interview") with

Applicants' representative Adriane M. Antler. During the Third Interview, SPE Shukla confirmed the suggestions for claim amendments he had provided in the Second Interview, saying that such would "go a long way" towards achieving allowance of the application although Examiner Lu would need to conduct a new search. SPE Shukla stated that, due to his time restrictions, SPE Shukla would not be able to interview the case with Applicants or Applicants' representatives prior to October 31, 2007. Ms. Antler advised SPE Shukla that Applicants proposed to file a Request for Continued Examination ("RCE") with their Response to the Office Action, and that October 31, 2007 was the deadline for filing a RCE for the application, in view of the new Patent and Trademark Office rules. Accordingly, SPE Shukla suggested that Applicants file the RCE with the Response by October 31, 2007 and then have a telephonic interview with SPE Shukla and Examiner Lu the week of November 5, 2007, after which, if desired, a Supplemental Amendment could be filed. Accordingly, SPE Shukla agreed to conduct a telephonic interview on November 6, 2007 at 3:00 pm ET with Ms. Antler.

Applicants further thank SPE Shukla and Examiner Lu for the courtesies extended during the telephone interview on November 6, 2007 (hereinafter "the Fourth Interview") with representatives of Assignee Eileen Sun, John Castle and Applicants' representatives Adriane M. Antler and Stephanie X. Wang. During the Fourth Interview, SPE Shukla suggested that claims 1, 284, and 285 be amended further for clarity. In particular, SPE Shukla recommended that claims 1, 284, and 285 be amended essentially as set forth hereinabove, and indicated that such amendments would overcome the rejection of record under 35 U.S.C. § 112.

**THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE  
WITHDRAWN**

The Examiner rejected claims 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265, 280-283, and 293-296 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully disagree with the Examiner's rejection.

First, the Examiner contends that:

since claims 1, 10, 284, and 285 do not require that each of the plurality of different genes or a sample comprising RNAs or nucleic acids contains different splicing forms, when a gene in the plurality of different genes or RNAs or nucleic acids does not contain different splicing forms, it is unclear how to differentiate the nucleic acid expression level of a whole gene from the nucleic acid expression level of individual exons or individual multiexons of the whole gene using real-time RT-PCR or nucleic acid arrays.

(Office Action, page 3, third paragraph).

Applicants respectfully point out that claim 1 as previously pending recited that “at least one gene in said plurality of different genes has an exon having a plurality of different variants.” Claim 1 as currently amended recites “measuring... the nucleic acid expression levels of a plurality of different variants of an exon of a gene, for each gene in said plurality of different genes.” The claim as amended also specifies that the plurality of probes on the array “comprises a probe that specifically hybridizes to one of said different variants of an exon of a gene, for each gene in said plurality of different genes.” As such, the Examiner's contention has no basis. When the particular splice form of an exon variant being measured is not present in the nucleic acid sample, the measured expression level will be zero. If the splice form is present, the measured expression level will be greater than zero. Either way, the claim is enabled. Claim 10 has been cancelled. Regarding claims 284 and 285, amended claims 284 and 285 both recite methods for analyzing expression levels of exon variants of a plurality of different genes by using probes that comprise “a variant junction probe for each of a plurality of different variants of at least one exon for each gene in said plurality of different genes.” As such, the Examiner's contention regarding claims 284 and 285 also has no basis. When the particular splice form of an exon variant being measured is not present in the cell sample, the measured expression level will be zero. If the splice form is present, the measured expression level will be greater than zero. Either way, claims 284 and 285 are enabled. Accordingly, the Examiner's first contention for rejecting claims 1, 4-34, 36, 45,

86, 87, 89, 90, 157-181, 183, 263-265, 280-283, and 293-296 is unfounded.

Second, the Examiner contends that:

since claim 10 does not require that the polynucleotide probes on the positionally-addressable array contains probes which hybridize to different splicing forms of the at least one gene recited in claim 1, it is unclear how to measuring [sic], in vitro, the nucleic acid expression level of each of said plurality of different variants of said exon in said at least one gene as recited in claim 1.

(Office Action, page 3, fourth paragraph bridging to page 4, first paragraph).

Applicants respectfully point out the following language in amended claim 1: “wherein said plurality of polynucleotide probes comprises a probe that specifically hybridizes to one of said different variants of an exon of a gene, for each gene in said plurality of different genes.” Accordingly, the Examiner’s contention has no basis, since the expression levels of the different variants of the exon can be measured by using the probes recited in amended claim 1. As such, the Examiner’s second contention is also unfounded.

Third, the Examiner contends that:

although claims 284 and 285 are directed to a method for analyzing exon expression, since there is no method step for analyzing exon expression in the claim, it is unclear how to analyze exon expression.

(Office Action, page 4, second paragraph).

Applicants respectfully submit that claims 284 and 285 are both drawn to analyzing exon expression based on methods comprising a contacting step (a) and a measuring step (b), which provide the analysis of exon expression. As such, the Examiner’s third contention is also unfounded.

Accordingly, Applicants respectfully request that the rejections of claims 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265, 280-283, and 293-296 under 35 U.S.C. § 112, first paragraph, be withdrawn.

### CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

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Respectfully submitted,

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